What is claimed is:

1. A polynucleotide encoding a recombinant polypeptide comprising an organelle localization signal and a protein transduction domain.

2. The polynucleotide of claim 1, wherein the organelle localization signal is operably linked to the protein transduction domain.

3. The polynucleotide of claim 1, wherein the recombinant polypeptide comprises a cleavage site for removing the protein transduction domain.

4. The polynucleotide of claim 1, wherein the protein transduction domain is positioned within the recombinant polypeptide to be cleaved within a targeted organelle.

5. The polynucleotide of claim 1, wherein the recombinant polypeptide comprises a viral polypeptide.

6. The polynucleotide of claim 5, wherein the viral polypeptide comprises a viral surface polypeptide.

7. The polynucleotide of claim 6, wherein the viral surface polypeptide comprises a bacteriophage surface polypeptide.

8. The polynucleotide of claim 7, wherein the bacteriophage surface polypeptide comprises bacteriophage lambda surface polypeptide .

9. The polynucleotide of claim 7, wherein the viral surface polypeptide is selected from the group consisting of capsid and tail proteins.

10. The polynucleotide of claim 6, wherein the viral surface peptide comprises between 80-100% homology to gpD (SEQ. ID NO. 5).

11. The polynucleotide of claim 1, wherein the organelle localization signal comprises a mitochondrial localization signal.

12. The polynucleotide of claim 11, wherein the mitochondrial localization signal comprises a sequence having 80-100% homology to a mitochondrial localization signal selected from the group consisting of hexokinase I, amine oxidase (flavin-containing) A, hexokinase IV, pancreatic beta cell form, peripheral benzodiazepine receptor-related protein, metaxin 2, putative mitochondrial outer membrane protein import receptor (hTOM), glutathione transferase; voltage-dependent anion channel 2 (outer mitochondrial membrane protein porin), hexokinase IV, cytochrome b5, peripheral benzodiazepine receptor, germ cell kinase anchor S-AKAP84, A kinase anchor protein, carnitine O-palmitoyltransferase I precursor, hexokinase II, amine oxidase (flavin-containing) B, long-chain-fatty-acid--CoA ligase 2, long-chain-fatty-acid--CoA ligase 1 (palmitoyl-CoA ligase), voltage-dependent anion channel 1, metaxin 1, Human putative outer mitochondrial membrane 34 kDa translocase hTOM34, voltage-dependent anion channel 4 (outer mitochondrial membrane protein porin), cytochrome-b5 reductase, voltage-dependent anion channel 3 (outer mitochondrial membrane protein porin), Mitochondrial import receptor subunit TOM20 homolog (Mitochondrial 20 kd outer membrane protein) (Outer mitochondrial membrane receptor TOM20), tumorous imaginal discs homolog precursor (HTID-1), and SEQ. ID Nos. 7-177.

13. The polynucleotide of claim 1, wherein the protein transduction domain comprises a plurality of amino acid residues having a net positive charge under physiological conditions.

14. The polynucleotide of claim 1, wherein the protein transduction domain comprises 8-15 amino acid residues.

15. The polynucleotide of claim 1, wherein the protein transduction domain comprises 11 arginine residues.

16. The polynucleotide of claim 1, wherein the protein transduction domain RKKRRQRRR (SEQ. ID. NO. 4).

17. A recombinant polypeptide comprising an organelle localization signal and a protein transduction domain.

18. The recombinant polypeptide of claim 17, wherein the organelle localization signal is operably linked to the protein transduction domain.

19. The recombinant polypeptide of claim 17, wherein the recombinant polypeptide comprises a cleavage site for removing the protein transduction domain.

20. The recombinant polypeptide of claim 17, wherein the protein transduction domain is positioned within the recombinant polypeptide to be cleaved within a targeted organelle.

21. The recombinant polypeptide of claim 17, wherein the recombinant polypeptide is operably linked to a vector.

22. The recombinant polypeptide of claim 17, wherein the vector comprises a viral vector.

23. The recombinant polypeptide of claim 22, wherein the viral vector comprises a bacteriophage vector.

24. The recombinant polypeptide of claim 23, wherein the bacteriophage vector comprises a lambda bacteriophage vector.

25. The recombinant polypeptide of claim 17, wherein the recombinant polypeptide is located on a surface of the vector.

26. The recombinant polypeptide of claim 17, wherein the protein transduction domain enables the recombinant polypeptide to cross a cell membrane.

27. The recombinant polypeptide of claim 17, wherein the organelle localization signal directs the recombinant polypeptide to a specific organelle.

28. A polynucleotide encoding a recombinant polypeptide, wherein the recombinant polypeptide comprises a chloroplast localization signal and a protein transduction domain.

29. The polynucleotide of claim 28, wherein the organelle localization signal is operably linked to the protein transduction domain.

30. The polynucleotide of claim 28, wherein the recombinant polypeptide comprises a cleavage site for removing the protein transduction domain.

31. The polynucleotide of claim 28, wherein the protein transduction domain is positioned within the recombinant polypeptide to be cleaved within a targeted organelle.

32. The polynucleotide of claim 28, wherein the recombinant polypeptide comprises a viral polypeptide.

33. The polynucleotide of claim 32, wherein the viral polypeptide comprises a viral surface polypeptide.

34. The polynucleotide of claim 33, wherein the viral surface polypeptide comprises a bacteriophage surface polypeptide.

35. The polynucleotide of claim 34, wherein the bacteriophage surface polypeptide comprises a bacteriophage lambda surface polypeptide.

36. The polynucleotide of claim 28, wherein the chloroplast localization signal has 80-100% homology to a chloroplast localization signal selected from the group consisting of transit peptide domain of the apicoblast ribosomal protein S9, Pea glutathione reductase (GR) signal peptide, NH2-terminus of Cr-RSH encoding a putative guanosine 3',5'-bispyrophosphate (ppGpp) synthase-degradase, 14-3-3 proteins, chloroplast signal recognition particle including cpSRP54, cpSRP43 subunits or a fragment thereof, chloroplast transit peptides AtOEP7 including transmembrane domain (TMD) and its C-terminal neighboring seven-amino acid region, THI1 N-terminal chloroplastic transit peptide, and SEQ. ID Nos. 178-194.

37. The polynucleotide of claim 33, wherein the viral surface polypeptide comprises a polypeptide having 80-100% homology to gpD (SEQ. ID NO. 5)

38. The polynucleotide of claim 28, wherein the protein transduction domain comprises a plurality of amino acid residues having a net positive charge under physiological conditions.

39. The polynucleotide of claim 28, wherein the protein transduction domain comprises 8-15 amino acid residues.

40. The polynucleotide of claim 28, wherein the protein transduction domain comprises 11 arginine residues.

41. A recombinant viral vector comprising the polynucleotide of claim 1.

42. The recombinant viral vector of claim 41, wherein the vector comprises a bacteriophage vector.

43. The recombinant viral vector of claim 42, wherein the vector comprises a lambda bacteriophage vector.

44. A cell comprising a modified organelle, wherein said modified organelle comprises a bacteriophage.

45. The cell of claim 44, wherein the organelle is selected from the group consisting of a mitochondrion and a chloroplast.

46. The cell of claim 44, wherein the cell comprises a eukaryotic cell.

47. The cell of claim 44, wherein the bacteriophage comprises lambda bacteriophage.

48. The cell of claim 44, where the bacteriophage is a recombinant bacteriophage.

49. The cell of claim 44, wherein the bacteriophage comprises a polynucleotide encoding a mitochondrial localization signal and a protein transduction domain.

50. The cell of claim 44, wherein the bacteriophage comprises a polynucleotide encoding a chloroplast localization signal and a protein transduction domain.

51. The cell of claim 44, wherein the chloroplast localization signal has 80-100% homology to a chloroplast localization signal selected from the group consisting of transit peptide domain of the apicoblast ribosomal protein S9, Pea glutathione reductase (GR) signal peptide, NH2-terminus of Cr-RSH encoding a putative guanosine 3',5'-bispyrophosphate (ppGpp) synthase-degradase, 14-3-3 proteins, chloroplast signal recognition particle including cpSRP54, cpSRP43 subunits or a fragment thereof, chloroplast transit peptides AtOEP7 including transmembrane domain (TMD) and its C-terminal neighboring seven-amino acid region, THI1 N-terminal chloroplastic transit peptide, and SEQ. ID Nos. 178-194.

52. The cell of claim 49, wherein the protein transduction domain comprises a plurality of amino acid residues having a net positive charge under physiological conditions.

53. The cell of claim 49, wherein the protein transduction domain comprises 8-15 amino acid residues.

54. The cell of claim 49, wherein the protein transduction domain comprises 11 arginine residues.

55. A method of transfecting a cell, said method comprising the step of:

contacting the cell with a vector operably linked to a polypeptide, the polypeptide comprising a protein transduction domain and an organelle targeting signal.

56. The method of claim 55, wherein the vector expresses the polypeptide on a surface of the vector.

57. The method of claim 56, wherein the vector traverses the cell's outer membrane via the protein transduction domain.

58. The method of claim 57, wherein said organelle targeting signal directs the vector to a specific organelle.

59. The method of claim 58, wherein the vector traverses a membrane of the specific organelle.

60. The method of claim 55, wherein the organelle targeting signal is specific for mitochondria or chloroplasts.

61. The method of claim 55, wherein the vector comprises a viral vector.

62. The method of claim 61, wherein the viral vector comprises a bacteriophage vector.

63. The method of claim 62, wherein the bacteriophage vector comprises a lambda bacteriophage vector.

64. The method of claim 55, wherein the organelle targeting signal has 80-100% homology to an organelle targeting signal selected from the group consisting of hexokinase I, amine oxidase (flavin-containing) A, hexokinase IV, pancreatic beta cell form, peripheral benzodiazepine receptor-related protein, metaxin 2, putative mitochondrial outer membrane protein import receptor (hTOM), glutathione transferase; voltage-dependent anion channel 2 (outer mitochondrial membrane protein porin), hexokinase IV, cytochrome b5, peripheral benzodiazepine receptor, germ cell kinase anchor S-AKAP84, A kinase anchor protein, carnitine O-palmitoyltransferase I precursor, hexokinase II, amine oxidase (flavin-containing) B, long-chain-fatty-acid--CoA ligase 2, long-chain-fatty-acid--CoA ligase 1 (palmitoyl-CoA ligase), voltage-dependent anion channel 1, metaxin 1, Human putative outer mitochondrial membrane 34 kDa translocase hTOM34, voltage-dependent anion channel 4 (outer mitochondrial membrane protein porin), cytochrome-b5 reductase, voltage-dependent anion channel 3 (outer mitochondrial membrane protein porin), Mitochondrial import receptor subunit TOM20 homolog (Mitochondrial 20 kd outer membrane protein) (Outer mitochondrial membrane receptor TOM20), tumorous imaginal discs homolog precursor (HTID-1), transit peptide domain of the apicoblast ribosomal protein S9, Pea glutathione reductase (GR) signal peptide, NH2-terminus of Cr-RSH encoding a putative guanosine 3',5'-bispyrophosphate (ppGpp) synthase-degradase, 14-3-3 proteins, chloroplast signal recognition particle including cpSRP54, cpSRP43 subunits or a fragment thereof, chloroplast transit peptides AtOEP7 including transmembrane domain (TMD) and its C-terminal neighboring seven-amino acid region, THI1 N-terminal chloroplastic transit peptide, and SEQ. ID NOs. 7-194.

65. The method of claim 55, wherein the protein transduction domain comprises a plurality of amino acid residues having a net positive charge under physiological conditions.

66. The method of claim 55, wherein the protein transduction domain comprises 8-15 amino acid residues.

67. The method of claim 55, wherein the protein transduction domain comprises 11 arginine residues.

66. A method of modifying an organelle, the method comprising the step of

transfecting the cell with a recombinant lambdaphage, the recombinant lambdaphage comprising a polynucleotide encoding an organelle localization signal operably linked to a bacteriophage lambda surface protein;

wherein the organelle localization signal is displayed on a surface of the recombinant lambdaphage and directs the recombinant lambdaphage to the organelle; and

wherein the recombinant lambdaphage introduces a polynucleotide into the organelle.

67. The method of claim 66, wherein the organelle is a mitochondrion, and the organelle localization signal comprises at least a fragment of subunit VIII of human cytochrome oxidase.

68. A kit for transfecting organelles, the kit comprising:

a polynucleotide encoding an organelle localization signal operably linked to a bacteriophage lambda surface polypeptide; and

bacteriophage lambda packaging components for preparing a recombinant lambda vector.

69. The kit of claim 68, wherein the localization signal comprises a chloroplast localization signal.

70. The kit of claim 68, wherein the localization signal comprises a mitochondrial localization signal.

71. The kit of claim 68, wherein the localization signal comprises at least a fragment of subunit VIII of human cytochrome oxidase.

72. A system for transfecting organelles, said system comprising

a polynucleotide encoding an organelle localization signal peptide operably linked to a bacteriophage surface polypeptide; and

a recombinant bacteriophage vector.

73. A method for transfecting organelles, the method comprising the step of

introducing a recombinant viral vector into the cytosol of a cell, wherein the recombinant viral vector displays an organelle localization signal on a surface of the vector for directing the vector to an organelle to be transfected.

74. The method of claim 73, wherein the recombinant viral vector is lambda bacteriophage and said organelle localization signal has 80-100% homology to an organelle localization signal selected from the group consisting of hexokinase I, amine oxidase (flavin-containing) A, hexokinase IV, pancreatic beta cell form, peripheral benzodiazepine receptor-related protein, metaxin 2, putative mitochondrial outer membrane protein import receptor (hTOM), glutathione transferase; voltage-dependent anion channel 2 (outer mitochondrial membrane protein porin), hexokinase IV, cytochrome b5, peripheral benzodiazepine receptor, germ cell kinase anchor S-AKAP84, A kinase anchor protein, carnitine O-palmitoyltransferase I precursor, hexokinase II, amine oxidase (flavin-containing) B, long-chain-fatty-acid--CoA ligase 2, long-chain-fatty-acid--CoA ligase 1 (palmitoyl-CoA ligase), voltage-dependent anion channel 1, metaxin 1, Human putative outer mitochondrial membrane 34 kDa translocase hTOM34, voltage-dependent anion channel 4 (outer mitochondrial membrane protein porin), cytochrome-b5 reductase, voltage-dependent anion channel 3 (outer mitochondrial membrane protein porin), Mitochondrial import receptor subunit TOM20 homolog (Mitochondrial 20 kd outer membrane protein) (Outer mitochondrial membrane receptor TOM20), tumorous imaginal discs homolog precursor (HTID-1), transit peptide domain of the apicoblast ribosomal protein S9, Pea glutathione reductase (GR) signal peptide, NH2-terminus of Cr-RSH encoding a putative guanosine 3',5'-bispyrophosphate (ppGpp) synthase-degradase, 14-3-3 proteins, chloroplast signal recognition particle including cpSRP54, cpSRP43 subunits or a fragment thereof, chloroplast transit peptides AtOEP7 including transmembrane domain (TMD) and its C-terminal neighboring

seven-amino acid region, THI1 N-terminal chloroplastic transit peptide, and SEQ. ID Nos. 7-194.

75. A composition comprising a recombinant polypeptide comprising an organelle localization signal operably linked to a protein transduction domain, wherein the recombinant polypeptide is operably linked to a polynucleotide.

76. A method for modifying the metabolism of a cell, the method comprising:

contacting the cell with a recombinant vector displaying a recombinant polypeptide comprising a mitochondrial localization signal operably linked to a protein transduction domain, the recombinant vector comprising a polynucleotide encoding a functional respiratory chain component, wherein the functional respiratory chain component compensates for the at least one defective respiratory chain component when expressed by the cell.

77. The method of claim 76, wherein the functional respiratory chain component is expressed in at least one mitochondrion of the cell.

78. The method of claim 76, wherein the vector encodes the recombinant polypeptide displayed on the surface of the vector.

79. The method of claim 78, wherein the vector traverses the cell's outer membrane via the protein transduction domain.

80. The method of claim 76, wherein the cell is a eukaryotic cell.

81. A method for modifying cytochrome oxidase activity in a cell, the method comprising:

contacting the cell with a recombinant vector displaying a recombinant polypeptide comprising a mitochondrial localization signal operably linked to a protein transduction domain, the recombinant vector encoding a functional cytochrome oxidase subunit, wherein the functional cytochrome oxidase subunit modifies cytochome oxidase activity of the cell.

82. The method of claim 81, wherein the functional cytochrome oxidase subunit is expressed in at least one mitochondrion of the cell.

83. The method of claim 81, wherein the vector encodes the recombinant polypeptide displayed on a surface of the vector.

84. The method of claim 81, wherein the vector traverses the cell's outer membrane via the protein transduction domain.

85. A method for compensating for a mtDNA mutation in a host, the method comprising the steps of:

contacting a host's cell having a mtDNA mutation with a recombinant vector expressing a recombinant polypeptide comprising a mitochondrial localization signal operably linked to a protein transduction domain, the recombinant vector also encoding a functional product corresponding to the mtDNA mutation.

86. The method of claim 84, wherein the contacting occurs in vivo or in vitro.

87. The method of claim 84, wherein the vector expresses the recombinant polypeptide on a surface of the vector.

88. The method of claim 84, wherein the vector traverses the cell's outer membrane via the protein transduction domain.

89. A recombinant bacteriophage comprising a modified surface polypeptide, wherein the modified surface polypeptide comprises a protein transduction domain.

90. A recombinant bacteriophage comprising a modified surface polypeptide, wherein the modified surface polypeptide comprises an organelle localization signal.

91. A recombinant bacteriophage comprising a modified surface polypeptide, wherein the modified surface polypeptide comprises a protein transduction domain operably linked to an organelle localization signal.

92. A method of treating a mitochondrial disease in a host comprising:

contacting a host's cell with a recombinant vector displaying a recombinant polypeptide comprising a mitochondrial localization signal operably linked to a protein transduction domain, the recombinant vector encoding a functional mitochondrial polypeptide, wherein the recombinant vector transfects at least one of the host's mitochondria enabling the host's cell to express the functional mitochondrial polypeptide in the at least one transfected mitochondrion.

93. The method of claim 84, wherein the contacting occurs in vivo or in vitro.

94. The method of claim 91, wherein the mitochondrial disease is selected from the group consisting of Alpers Disease; Barth syndrome; β-oxidation defects; carnitine-acyl-carnitine deficiency; carnitine deficiency; co-enzyme Q10 deficiency; Complex I deficiency; Complex II deficiency; Complex III deficiency; Complex IV deficiency; Complex V deficiency; cytochrome c oxidase (COX) deficiency; Chronic Progressive External Ophthalmoplegia Syndrome (CPEO); CPT I Deficiency; CPT II deficiency; Glutaric Aciduria Type II; lactic acidosis; Long-Chain Acyl-CoA Dehydrongenase Deficiency (LCAD); LCHAD; mitochondrial cytopathy; mitochondrial DNA depletion; mitochondrial encephalopathy; mitochondrial myopathy; Mitochondrial Encephalomyopathy with Lactic Acidosis and Strokelike episodes (MELAS); Myoclonus Epilepsy with Ragged Red Fibers (MERRF); Maternally Inherited Leigh's Syndrome (MILS); Myogastrointestinal encephalomyopathy (MNGIE); Neuropathy, ataxia and retinitis pigmentosa (NARP); Leber's Hereditary Optic Neuropathy (LHON); Progressive external ophthalmoplegia (PEO); Pearson syndrome; Kearns-Sayre syndrome (KSS); Leigh's syndrome; intermittent dysautonomia; pyruvate carboxylase deficiency; pyruvate dehydrogenase deficiency; respiratory chain mutations and deletions; Short-Chain Acyl-CoA Dehydrogenase Deficiency (SCAD); SCHAD; and Very Long-Chain Acyl-CoA Dehydrongenase Deficiency (VLCAD).

95. A method for producing a mtDNA depleted cell comprising:
contacting the cell with at least one siRNA directed to POLγ.

96. The method of claim 95, wherein the siRNA is selected from the siRNAs listed in TABLE 3 or a sequence having 80-100% homology to the siRNAs listed in TABLE 3 or SEQ ID NOs. 195-574.

97. The method of claim 95, wherein a target sequence of POLγ RNA inhibition is selected from the POLγ target sequences in TABLE 3.

98. A method of depleting mtDNA in a cell comprising:
contacting the cell with an inhibitor of mtDNA replication or transcription.

99. The method of claim 98, wherein the inhibitor of mtDNA replication is an antisense polynucleotide or a small inhibitory RNA.

100. The method of claim 98, wherein the inhibitor comprises DNA, RNA or a combination thereof.

101. The method of claim 98, wherein the inhibitor is selected from Table 3.

102. The method of claim 98, wherein the inhibitor is specific for a gene involved in mitochondrial DNA transcription or replication.

103. The method of claim 102, wherein the gene is selected from the group consisting of Polγ, TFAM A and B, and mtSSB.

104. The method of claim 102, wherein the gene encodes a mitochondrial polymerase.

105. A cell comprising an inhibitory polynucleotide that specifically binds to a polynucleotide encoding a mitochondrial polymerase.

106. A cell comprising an siRNA specific for a mitochondrial polymerase.

107. The cell of claim 106, wherein the mitochondrial polymerase comprises Polγ.

108. The cell of claim 106, wherein the siRNA is selected from the siRNAs listed in Table 3.

109. The cell of claim 105, wherein the inhibitory polynucleotide comprises an antisense polynucleotide.

110. The cell of claim 105, wherein the cell comprises a vector that expresses the inhibitory polynucleotide.

111 A cell comprising an inhibitory polynucleotide that specifically binds to a mitochondrial polymerase and inhibits the mitochondrial polymerase.

112. A virus particle comprising:

(a) a protein transduction domain operably linked to a surface of the virus particle;

(b) a targeting signal operably linked to a surface of the virus particle; and

(c) a polynucleotide.

113. A vector comprising:

a polynucleotide encoding a protein transduction domain operably linked to a targeting signal, wherein the protein transduction domain operably linked to the targeting signal is expressed on an exterior surface of the vector.